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- [54] **IONICALLY COVALENTLY CROSSLINKED AND CROSSLINKABLE BIOCOMPATIBLE ENCAPSULATION COMPOSITIONS AND METHODS**
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- [58] Field of Search 524/56, 54, 28; 424/488, 499; 435/177, 178

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References Cited

U.S. PATENT DOCUMENTS

4,177,038	12/1979	Biebricher et al.	435/178
4,352,883	10/1982	Lim	435/178
4,391,909	7/1983	Lim .	
4,409,331	10/1983	Lim .	
4,592,098	6/1986	Aurameas et al.	435/178
4,663,286	5/1987	Tsang et al. .	
4,744,933	5/1988	Rha et al. .	
4,749,620	6/1988	Rha et al. .	
4,791,061	12/1988	Sumino	435/178
4,798,786	1/1989	Tice	435/177
4,824,916	4/1989	Kershner et al.	525/420
5,041,292	8/1991	Feijin	424/488

FOREIGN PATENT DOCUMENTS

WO91/07951	6/1991	PCT Int'l Appl. .	
9109119	6/1991	PCT Int'l Appl.	435/178
WO91/11205	8/1991	PCT Int'l Appl. .	
2237574	5/1991	United Kingdom	524/28

OTHER PUBLICATIONS

Thesis re structural studies and the biosynthesis of alginates by Gudmund Skjak-Braek, Trondheim, Norway, Jun. 1988, (pp. I-VI and 1-49).

Article *Applications of some Algal Polysaccharides in Biotechnology*, by Gudmund Skjak-Braek & Anita Mar-

tinsen, Norwegian Institute of Technology, Trondheim, Norway, 1991 John Wiley & Sons, Ltd. (pp. 219-257).
"Alteration of Immunological Properties of Bovine Serum Albumin by Covalent Attachment of Polyethylene Glycol" by Abraham Abuchowski, Theo van Es, Nicholas C. Palczuk and Frank F. Davis, *Journal of Biological Chemistry*, vol. 252, No. 11, Jun. 1977, pp. 3578-3581.

"Surface Topography Of Crosslinked Poly(ethylene oxide)/polysiloxane networks in the dry and hydrated states" by Elliott L. Chaikof, Edward W. Merrill, Sylvie L. Verdon, Lori L. Hayes, Raymond J. Connolly and Allan D. Callow, *Polymer Communications*, 1990, vol. 31, May, pp. 182-185.

"Synthesis of ionic conducting interpenetrating polymer networks" by Chiang, Bauer, Briber and Davis, *Polymer Communications*, 1987, vol. 28, Feb. pp. 34-36.

"Synthetic hyrogels: 7. High EWC semi-interpenetrating polymer networks based on cellulose esters and N-containing hydrophilic monomers" by Corkhill and Tighe, *Polymer Communications*, 1990, vol. 31, Aug. pp. 1526-1537.

(List continued on next page.)

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ABSTRACT

Crosslinked biocompatible compositions comprising an ionically crosslinked component and a covalently crosslinked component for encapsulating biologics are disclosed. In accordance with the present invention, also disclosed are crosslinkable biocompatible mixtures comprising an ionically crosslinkable component and a covalently crosslinkable component. Methods for encapsulating biologics with the crosslinked and crosslinkable biocompatible compositions are provided. Also, retrievable macrocapsules for encapsulating microcapsules or biologics are disclosed.

36 Claims, 8 Drawing Sheets

